FAMILY PRACTICE

Management of acute strychnine poisoning

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Acute strychnine poisoning, although relatively rare, must be distinguished from epilepsy, tetanus, meningitis, hysteria and phenothiazine intoxication. Management requires (a) maintenance of a protected airway and monitoring of respiration, (b) control of "spinal convulsions", (c) correction of anion gap and other electrolyte imbalances, (d) blockage of strychnine absorption and (e) enhancement of strychnine excretion.

Strychnine is an agent of no known therapeutic value. However, acute intoxication with it may occur because it is readily available as a rodenticide. We will describe the treatment of a patient who had a seizure due to strychnine intoxication and discuss how life-threatening metabolic acidosis can be reversed with specific and appropriate supportive treatment.

Case report

Clinical course

A 34-year-old woman with a personality disorder and a history of previous attempts at suicide was brought to the emergency room 30 minutes after ingesting a rodenticide containing approximately 340 mg of strychnine sulfate.

She was alert and apprehensive, and had frequent involuntary muscle contractions. During the initial assessment she had a tonic seizure, with generalized symmetric involvement of the major muscle groups and opisthotonic positioning. Spontaneous ventilation was maintained, and no cyanosis was present at any time. During the seizure the patient was acutely aware of her surroundings and frightened. Diazepam (10 mg) was administered intravenously. Following a period of voluntary hyperventilation, general anesthesia was induced with thiopental sodium (4 mg/kg of body weight) and muscular relaxation was obtained with succinylcholine chloride (1 mg/kg). Gastric lavage with saline was performed through a nasogastric tube, then a slurry of activated charcoal (25 g/dl of distilled water) and diluted potassium permanganate (1:5000 solution) were administered through the tube. A urinary catheter and cardiovascular monitoring devices (central venous pressure and intra-arterial cannulas) were inserted while the patient was anesthetized.

When she woke she was treated in a quiet, darkened room. Diuresis was induced with saline to enhance renal excretion of the strychnine. Her severe metabolic acidosis (Table I) was treated with a total of 134 mmol of sodium bicarbonate and her potassium deficiency with 120 mmol of potassium (as 9 g of potassium chloride), both given intravenously. Diazepam (a 2.5-mg bolus given intravenously every hour for 4 hours) was used to control the muscle spasms. A loading dose of phenytoin (10 mg/kg) was given intravenously at the rate of 50 mg/min.

In the 5 hours following the ingestion of strychnine the patient had heightened reflex excitability, as indicated by the spasms of the muscles of her neck, back and limbs produced by minimal sensory stimuli. Complete recovery, with no spasms, was evident 6 hours after admission.

Table I—Arterial blood gas and electrolyte levels in a patient with acute strychnine poisoning

Variable in arterial blood	Upon arrival at emergency room	Time (h) after arrival			
		½*	1*	1½	8
Sodium, mmol/l	148	139	139	142	142
Potassium, mmol/l	3.5	4.2	3.5	2.7	4.1
Chloride, mmol/l	103	102	103	110	109
Bicarbonate, mmol/l	9	4	16	20	24
Anion gap, mmol/l	36	33	20	12	9
pH	–	7.02	7.33	7.36	7.41
Oxygen tension, mm Hg	–	115	169	91	112
Carbon dioxide tension, mm Hg	–	20	32	32	36

*While the patient was receiving oxygen at a rate of 4 l/min.

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Laboratory investigation

Blood was drawn anaerobically from a cannula in the radial artery into an iced syringe containing heparin. Blood gas and electrolyte levels were measured immediately on a Corning 175 blood gas analyser and a Technicon II AutoAnalyzer. The anion gap was calculated by subtracting the sum of the serum chloride and serum bicarbonate levels from the serum sodium level.[1] The normal anion gap is 12 ± 2 mmol/l. The levels of metabolic intermediates were measured enzymatically on perchloric acid extracts of whole blood,[2] the serum phosphate level was determined as described by Fiske and SubbaRow,[3] and the strychnine level in basic extracts of urine was determined qualitatively by thin-layer chromatography with an iodoplatinate spray.[4]

There was no clinical or biochemical evidence of hepatic, renal or hematologic abnormalities. The electrolyte and arterial blood gas analysis revealed an anion-gap type of metabolic acidosis; with treatment it resolved in 6 hours (Table I). Thirty minutes after the patient's arrival in the emergency room the blood lactate concentration was 10 mmol/l (normal value less than 1 mmol/l) but the blood levels of salicylate, β-hydroxybutyrate, acetoacetate, citrate, acetate and phosphate were normal. Urine samples collected 2 and 8 hours after the patient's arrival were found to contain strychnine.

Discussion

Strychnine is the prototype of chemicals that selectively block postsynaptic inhibitory neurons in the central nervous system and, hence, increase the level of neuronal excitability.[5]

The interaction of benzodiazepines, in this case diazepam, with the receptors for γ-aminobutyric acid (GABA), the universal inhibitory transmitter in the brain and a mediator of presynaptic inhibition in the spinal cord, may be responsible for the effectiveness of these drugs in the treatment of acute strychnine intoxication. In reviewing the mechanism of action of benzodiazepines Costa and Guidotti[6] concluded that these drugs act similarly to GABA on all physiologic inhibitory mechanisms known to be mediated by this substance. Benzodiazepines have no direct GABA-mimetic effect, but by increasing the affinity of the GABA receptors they increase the efficiency of synaptic inhibitory transmission.

Specific binding of radioactively labelled strychnine at similar receptor sites has been demonstrated in the mammalian spinal cord, thalamus and brain stem.[7] Because of this postulated locus of action the seizure-like activity in strychnine intoxication has been termed "spinal convulsions".[8] When neuronal inhibition is blocked by strychnine, sensory stimuli (tactile, auditory or visual) can produce exaggerated reflex effects, as in our patient. Neuronal systems lacking specific synaptic inhibitory fibres are not excited by strychnine; thus, the cardiovascular and gastrointestinal systems are not directly affected by this agent.

Our patient exhibited muscle twitching and spasms as well as a tonic seizure in response to sensory stimuli. This syndrome in a conscious patient is characteristic, but not pathognomonic, of strychnine poisoning. The clinician must differentiate this condition from epilepsy, tetanus, meningitis, hysteria and phenothiazine intoxication.

Strychnine is absorbed very rapidly from the gastrointestinal system.[8,9] There is very little plasma protein binding, and the drug is rapidly cleared from the blood.[8,9] Thus, study of the gastric lavage fluid and of blood will not be of diagnostic help. However, up to 20% of an ingested dose is excreted unchanged in the urine, 70% in the first 6 hours,[8,10] so strychnine poisoning can be reliably identified from study of the urine, particularly in those first 6 hours. Strychnine is metabolized mainly by the microsomal enzyme system of the liver,[11] and inducers of this system have protected against toxic effects in animals given several minimum lethal doses of the drug.

The principles of management of strychnine intoxication are similar to those of any acute poisoning.[8,12] Absorption of the drug may be prevented by the early use of gastric lavage with saline, activated charcoal and potassium permanganate, although first any seizures must be controlled and the airway protected. Activated charcoal is a potent absorbent that rapidly binds many poisons, including strychnine.[12] Potassium permanganate, an oxidizing agent, reacts with many organic substances, including strychnine; because it is an irritant, a solution no stronger than 1:5000 should be used.[12] Peritoneal dialysis and hemodialysis appear to be of little benefit because of strychnine's rapid clearance from the blood.

The reflex hyperexcitability associated with acute strychnine poisoning means that any manipulation (gastric lavage, insertion of monitoring aids or peritoneal dialysis) should be done with total control of the airway. This often necessitates general anesthesia and endotracheal intubation. Our experience and that of others suggest that diazepam provides the most effective control of strychnine-induced hyperexcitability and seizure activity, thus allowing adequate spontaneous ventilation.[8,13,14] Recent studies leave little doubt, however, that in many patients diazepam significantly depresses respiration,[15] and in patients with a life-threatening metabolic acidosis any depression of the normal mechanism for compensatory hyperventilation can be lethal. Therefore, patients being treated with diazepam must be observed closely while the acidosis is being treated.

The most striking feature of our case was the severe metabolic acidosis of the anion-gap type. Lactic acidemia accounted for most of the metabolic acidosis. Increases in the blood lactate level to 22 mmol/l have been noted with strenuous exercise and with seizure activity[16,17] and probably reflect enhanced lactic acid production in muscle due to severe and prolonged muscular activity (i.e., a relative oxygen deficit). There was never any clinical evidence in our patient of arterial hypoxia, hypotension or hypoperfusion.

The most important aspect of treating this form of lactic acidosis is controlling muscular activity (with

diazepam in this case) and maintaining adequate ventilation. Our patient was given sodium bicarbonate intravenously because of the severe acidemia. Complete correction of the bicarbonate deficit is not necessary in such cases, as the metabolism of lactate generates bicarbonate.

The blood lactate concentration in our patient was 10 mmol/l when the calculated anion gap was 33 mmol/l. At this time the organic anion concentration in the serum (calculated by subtracting the measured anion gap from the normal anion gap) was 18 mmol/l. Most of the organic anions were lactate, their concentration being 10 mmol/l. The levels of other organic anions in the blood that were measured were not increased. The possibility of unidentified anions or unrecognized changes in the ionic equivalents of normal plasma constituents (proteins, calcium etc.) should be considered to account for this discrepancy. Gabow and colleagues[18] recently showed that such a discrepancy is common in patients treated for the anion-gap type of metabolic acidosis.

The high serum sodium concentration in the initial arterial blood sample from our patient may have been due to the mechanism proposed by Welt and associates.[19] They suggested that seizure activity produces intracellular hyperosmolarity, which causes water to shift into the cells so that the extracellular constituents become concentrated. The rise in the serum chloride level from 30 minutes to 8 hours was attributed to the infusion of isotonic saline in a patient with contraction of the extracellular fluid volume. The serum potassium concentration in the initial arterial sample was low, considering the associated metabolic acidosis, and in other cases of lactic acidosis after major seizures the serum potassium concentration has not been uniformly increased.[20] The reason for this has been reviewed by Halperin and coworkers.[21] No clinical or biochemical evidence of excessive renal or gastrointestinal loss of potassium was present initially in our patient. Persistence of her hypokalemia may partly be explained by excessive urinary loss associated with the saline-induced diuresis.

In summary, acute strychnine intoxication is a dramatic and readily treatable form of poisoning that requires prompt diagnosis and rapid institution of appropriate therapy.

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BOOKS

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